IN THE SPECIFICATION:

At page 1, lines 5-9, please replace the Related Applications paragraph with the following amended paragraph:

This application is a continuation application of U.S. Patent Application Serial No. 09/838,561, filed April 18, 2001, now U.S. Patent 6,627,423, issued September 30, 2003; which is a continuation-in-part of U.S. Patent Application Serial No. 09/816,760, filed March 23, 2001, now U.S. Patent 6,613,555, issued September 2, 2003, which is a continuation-in-part of U.S. Patent Application Serial No. 09/634,955, filed August 8, 2000, now U.S. Patent 6,511,834, issued January 28, 2003, which claims the benefit of U.S. Provisional Application Serial No. 60/192,002, filed March 24, 2000. The entire contents of all of the above-referenced applications are incorporated herein by this reference.

At page 3, lines 1-7, please replace the paragraph with the following amended paragraph:

In one embodiment, a DHDR nucleic acid molecule of the invention is at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 82%, 85%, 89%, 90%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, 99.99% or more identical to the nucleotide sequence (*e.g.*, to the entire length of the nucleotide sequence) shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____~~, PTA-1845, ~~_____~~, ~~_____~~, ~~or~~ ~~_____~~, or a complement thereof.

At page 3, line26, through page 4, line 33, please replace the paragraphs with the following amended paragraphs:

In another embodiment, a DHDR nucleic acid molecule includes a nucleotide sequence encoding a protein having an amino acid sequence sufficiently identical to the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____~~, PTA-1845, ~~_____~~, ~~_____~~, ~~or~~ ~~_____~~. In a preferred embodiment, a DHDR nucleic acid molecule includes a nucleotide sequence encoding a protein having an amino acid sequence at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, 99.99% or more identical to the entire length of the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____~~, PTA-1845, ~~_____~~, ~~_____~~, ~~or~~ ~~_____~~.

In another preferred embodiment, an isolated nucleic acid molecule encodes the amino acid sequence of human DHDR-1, DHDR-2, DHDR-3, or DHDR-4. In another preferred embodiment, an isolated nucleic acid molecule encodes the amino acid sequence of mouse DHDR-2. In yet another preferred embodiment, the nucleic acid molecule includes a nucleotide sequence encoding a protein having the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____. In yet another preferred embodiment, the nucleic acid molecule is at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000 or more nucleotides in length. In a further preferred embodiment, the nucleic acid molecule is at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000 or more nucleotides in length and encodes a protein having a DHDR activity (as described herein).

Another embodiment of the invention features nucleic acid molecules, preferably DHDR nucleic acid molecules, which specifically detect DHDR nucleic acid molecules relative to nucleic acid molecules encoding non-DHDR proteins. For example, in one embodiment, such a nucleic acid molecule is at least 20, 30, 40, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000 or more nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, or 14, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ or a complement thereof.

In preferred embodiments, the nucleic acid molecules are at least 15 (*e.g.*, 15 contiguous) nucleotides in length and hybridize under stringent conditions to the nucleotide molecules set forth in SEQ ID NO:1, 4, 7, 10, or 14.

In other preferred embodiments, the nucleic acid molecule encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____, wherein the nucleic acid molecule hybridizes to a complement of a nucleic acid molecule comprising SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16 under stringent conditions.

At page 5, lines 16 through 27, please replace the paragraph with the following amended paragraph:

In a preferred embodiment, a DHDR protein includes at least one or more of the following domains: a transmembrane domain, a signal peptide domain, an aldehyde dehydrogenase oxidoreductase domain, an aldehyde dehydrogenase family domain, a short chain dehydrogenase domain, an oxidoreductase protein dehydrogenase domain, a 3-beta hydroxysteroid dehydrogenase domain, a NAD-dependent epimerase/dehydratase domain, a short chain dehydrogenase/reductase domain, a shikimate 5-dehydrogenase domain, a dehydrogenase domain, and/or a glucose-1-dehydrogenase domain, and has an amino acid sequence at least about 50%, 55%, 60%, 65%, 67%, 68%, 70%, 75%, 80%, 85%, 90%, 92%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, 99.99% or more identical to the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____~~.

At page 6, lines 8 through 14, please replace the paragraph with the following amended paragraph:

In another embodiment, the invention features fragments of the protein having the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, wherein the fragment comprises at least 16 amino acids (*e.g.*, contiguous amino acids) of the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____~~. In another embodiment, a DHDR protein has the amino acid sequence of SEQ ID NO:2, 5, 8, 11, or 15.

At page 8, lines 12 through 17, please replace the paragraphs with the following amended paragraphs:

Figure 4 depicts the results of a search which was performed against the HMM database and which resulted in the identification of an "aldehyde dehydrogenase family domain" in the human DHDR-1 protein. The aldehyde dehydrogenase family domain (SEQ ID NO:17) is aligned with DHDR-1 protein (32142, SEQ ID NO:2).residues.

Figures 5A-5B depict the results of a search which was performed against the ProDom database and which resulted in the identification of a "aldehyde dehydrogenase oxidoreductase domain" in the human DHDR-1 protein (SEQ ID NO:2). The aldehyde dehydrogenase oxidoreductase domain (SEQ ID NO:18) is aligned with DHDR-1 protein (Sbjct, SEQ ID NO:2). residues.

At page 8, lines 29 through 34, please replace the paragraphs with the following amended paragraphs:

Figure 9 depicts the results of a search which was performed against the HMM database and which resulted in the identification of a "short-chain dehydrogenase domain" in the human DHDR-2 protein. The the short chain dehydrogenase domain (SEQ ID NO:19) is aligned with DHDR2 protein (21481; SEQ ID NO:5) residues.

Figure 10 depicts the results of a search which was performed against the ProDom database and which resulted in the identification of a "oxidoreductase protein dehydrogenase domain" in the human DHDR-2 protein (SEQ ID NO:5). The oxidoreductase protein dehydrogenase domain (SEQ ID NO:21) is aligned with DHDR2 protein residues.

At page 9, lines 8 through 14, please replace the paragraphs with the following amended paragraphs:

Figures 14A-14B depicts the results of a search which was performed against the HMM database and which resulted in the identification of a "3-beta hydroxysteroid dehydrogenase domain", a "short chain dehydrogenase domain", and a "NAD-dependent epimerase/dehydratase domain" in the human DHDR-3 protein. In Figure 14A, the short chain dehydrogenase domain (SEQ ID NO:19) is aligned with DHDR3 protein (25964; SEQ ID NO:8) residues. Also aligned is S-adenosylmethionine synthetase domain (SEQ ID NO:22) with DHDR3 protein residues. Figure 14B1 depicts an alignment of 3-betahydroxysteroid dehydrogenase domain (SEQ ID NO:23) with DHDR3 protein residues. Figure 14B2 depicts an alignment of NAD dependent epimerase/dehydratase domain (SEQ ID NO:24) with DHDR3 protein residues.

Figure 15 depicts the results of a search which was performed against the ProDom database and which resulted in the identification of a "3-beta hydroxysteroid dehydrogenase domain" in the human DHDR-3 protein (SEQ ID NO:8). The 3-beta hydroxysteroid dehydrogenase domain sequences (SEQ ID NO:25 and SEQ ID NO:26) is aligned with DHDR3 (Subjct) protein residues.

At page 9, lines 31 through 38, please replace the paragraphs with the following amended paragraphs:

Figure 20 depicts the results of a search which was performed against the HMM database and which resulted in the identification of a "short chain dehydrogenase domain" and a "short chain dehydrogenase/reductase domain" in the human DHDR-4 protein. The short chain dehydrogenase domain (SEQ ID NO:19) is aligned with DHDR4 protein (21686; SEQ ID NO:11) residues. Also, short chain dehydrogenase/reductase C2 domain (SEQ ID NO:27) is aligned with DHDR4 protein residues.

Figures 21A-21B depict the results of a search which was performed against the ProDom database and which resulted in the identification of a "oxidoreductase protein dehydrogenase domain" (SEQ ID NO:28, SEQ ID NO:29 and SEQ ID NO:30), a "shikimate 5-dehydrogenase domain"(SEQ ID NO:32), a "dehydrogenase domain"(SEQ ID NO:33) and a "glucose-1-dehydrogenase domain"(SEQ ID NO:31) in the human DHDR-4 protein (SEQ ID NO:11). Also depicted is alignment of a hypothetical protein domain (SEQ ID NO:34) aligned with human DHDR4 protein residues.

At page 23, line 27 through page 24, line 9, please replace the paragraph with the following amended paragraph:

The nucleotide sequence of the isolated human DHDR-1 cDNA and the predicted amino acid sequence of the human DHDR-1 polypeptide are shown in Figures 1A-1D and in SEQ ID NOs:1 and 2, respectively. The nucleotide sequence of the isolated human DHDR-2 cDNA and the predicted amino acid sequence of the human DHDR-2 polypeptide are shown in Figures 6A-6B and in SEQ ID NOs:4 and 5, respectively. The nucleotide sequence of the isolated human DHDR-3 cDNA and the predicted amino acid sequence of the human DHDR-3 polypeptide are shown in Figures 11A-11B and in SEQ ID NOs:7 and 8, respectively. The nucleotide sequence of the isolated human DHDR-4 cDNA and the predicted amino acid sequence of the human DHDR-4 polypeptide are shown in Figure 16 and in SEQ ID NOs:10 and 11, respectively. The nucleotide sequence of the isolated mouse DHDR-2 and the predicted amino acid sequence of the mouse DHDR-2 polypeptide are shown in Figures 31A and 31B, respectively, and in SEQ ID NOs:14 and 15, respectively. Plasmids containing the nucleotide sequence encoding human ~~DHDR-1,~~ DHDR-2~~, DHDR-3, and DHDR-4, and mouse DHDR-2~~ were deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on ~~_____,~~ May 9, 2000~~, _____, March 22, 2001, and _____, respectively~~, and assigned Accession ~~Numbers~~ Number ~~_____,~~ PTA-1845, ~~_____, _____, and _____, respectively~~. These deposits will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. These deposits were made merely as a convenience for those of skill in the art and are not an admission that deposits are required under 35 U.S.C. §112.

At page 25, lines 13 through 31, please replace the paragraph with the following amended paragraphs:

A nucleic acid molecule of the present invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845,

~~_____, _____, or _____,~~ or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or portion of the nucleic acid sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845, ~~_____, _____, or _____~~ as a hybridization probe, DHDR nucleic acid molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845, ~~_____, _____, or _____~~ can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845, ~~_____, _____, or _____~~.

At page 26, line 25 through page 28, line 2, please replace the paragraphs with the following amended paragraphs:

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845, ~~_____, _____, or _____,~~ or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845, ~~_____, _____, or _____,~~ is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~ PTA-1845, ~~_____, _____, or _____~~ such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, ~~_____, _____, or _____, respectively,~~ thereby forming a stable duplex.

In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 89%, 90%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, 99.99% or more identical to the entire length of the nucleotide

sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the entire length of the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____,~~ or a portion of any of these nucleotide sequences.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____,~~ for example, a fragment which can be used as a probe or primer or a fragment encoding a portion of a DHDR protein, *e.g.*, a biologically active portion of a DHDR protein. The nucleotide sequences determined from the cloning of the DHDR-1, DHDR-2, DHDR-3, and DHDR-4 genes allow for the generation of probes and primers designed for use in identifying and/or cloning other DHDR family members, as well as DHDR homologues from other species. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, or 75 consecutive nucleotides of a sense sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____~~ of an anti-sense sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____~~ or of a naturally occurring allelic variant or mutant of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____~~. In one embodiment, a nucleic acid molecule of the present invention comprises a nucleotide sequence which is greater than 50-100, 100-150, 150-200, 200-250, 250-300, 300-350, 350-400, 400-450, 450-500, 500-550, 550-600, 600-650, 650-700, 700-750, 750-800, 800-850, 850-900, 900-950, 950-1000, 1000-1050, 1050-1100, 1100-1150, 1150-1200, 1200-1250, 1250-1300, 1300-1350, 1350-1400, 1400-1450, 1450-1500, 1500-1550, 1550-1600, 1600-1650, 1650-1700, 1700-1750, 1750-1800, 1800-1850, 1850-1900, 1900-1950, 1950-2000 or more nucleotides in length and hybridizes under stringent hybridization conditions to a nucleic acid molecule of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____,~~PTA-1845, ~~_____, _____, or _____~~.

At page 28, lines 18 through 38, please replace the paragraphs with the following amended paragraphs:

A nucleic acid fragment encoding a "biologically active portion of a DHDR protein" can be prepared by isolating a portion of the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ which encodes a polypeptide having a DHDR biological activity (the biological activities of the DHDR proteins are described herein), expressing the encoded portion of the DHDR protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the DHDR protein.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ due to degeneracy of the genetic code and thus encode the same DHDR proteins as those encoded by the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NO:2, 5, 8, 11, or 15.

In addition to the DHDR nucleotide sequences shown in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the DHDR proteins may exist within a population (*e.g.*, the human population). Such genetic polymorphism in the DHDR genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules which include an open reading frame encoding a DHDR protein, preferably a mammalian DHDR protein, and can further include non-coding regulatory sequences, and introns.

At page 29, lines 21 through 32, please replace the paragraph with the following amended paragraph:

Moreover, nucleic acid molecules encoding other DHDR family members and, thus, which have a nucleotide sequence which differs from the DHDR sequences of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ are intended to be within the scope of the invention. For example, another DHDR cDNA can be identified based on the nucleotide sequence of human or mouse DHDR. Moreover, nucleic acid molecules encoding DHDR proteins from different species, and which, thus, have a nucleotide

sequence which differs from the DHDR sequences of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ are intended to be within the scope of the invention. For example, a mouse DHDR cDNA can be identified based on the nucleotide sequence of a human DHDR.

At page 30, lines 3 through 14, please replace the paragraph with the following amended paragraph:

Moreover, nucleic acid molecules encoding other DHDR family members and, thus, which have a nucleotide sequence which differs from the DHDR sequences of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ are intended to be within the scope of the invention. For example, another DHDR cDNA can be identified based on the nucleotide sequence of human or mouse DHDR. Moreover, nucleic acid molecules encoding DHDR proteins from different species, and which, thus, have a nucleotide sequence which differs from the DHDR sequences of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____ are intended to be within the scope of the invention. For example, a mouse DHDR cDNA can be identified based on the nucleotide sequence of a human DHDR.

At page 31, lines 21 through 38, please replace the paragraph with the following amended paragraph:

In addition to naturally-occurring allelic variants of the DHDR sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14 or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____, thereby leading to changes in the amino acid sequence of the encoded DHDR proteins, without altering the functional ability of the DHDR proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, or _____. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of DHDR (*e.g.*, the sequence of SEQ ID NO:2, 5, 8, 11, or 15) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are

conserved among the DHDR proteins of the present invention, *e.g.*, those present in a transmembrane domain, are predicted to be particularly unamenable to alteration. Furthermore, additional amino acid residues that are conserved between the DHDR proteins of the present invention and other members of the DHDR family are not likely to be amenable to alteration.

At page 32, lines 9 through 36, please replace the paragraph with the following amended paragraph:

An isolated nucleic acid molecule encoding a DHDR protein identical to the protein of SEQ ID NO:2, 5, 8, 11, or 15 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, ~~or~~ _____ such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, ~~or~~ _____ by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a DHDR protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a DHDR coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for DHDR biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, ~~or~~ _____, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

At page 34, line 37 through page 35, line14, please replace the paragraph with the following amended paragraph:

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haseloff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave DHDR mRNA transcripts to thereby inhibit translation of DHDR mRNA. A ribozyme having specificity for a DHDR-encoding nucleic acid can be designed based upon the nucleotide sequence of a DHDR cDNA disclosed herein (*i.e.*, SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____~~PTA-1845, ~~_____, _____, or _____~~). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a DHDR-encoding mRNA. See, *e.g.*, Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742. Alternatively, DHDR mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

At page 51, line 29 through page 52, line 16, please replace the paragraph with the following amended paragraph:

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haseloff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave DHDR mRNA transcripts to thereby inhibit translation of DHDR mRNA. A ribozyme having specificity for a DHDR-encoding nucleic acid can be designed based upon the nucleotide sequence of a DHDR cDNA disclosed herein (*i.e.*, SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ~~_____~~PTA-1845, ~~_____, _____, or _____~~). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a DHDR-encoding mRNA. See, *e.g.*, Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742. Alternatively, DHDR mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

At page 73, lines 22 through 34, please replace the paragraph with the following amended paragraph:

An exemplary method for detecting the presence or absence of DHDR protein or nucleic acid in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting DHDR protein or nucleic acid (*e.g.*, mRNA, or genomic DNA) that encodes DHDR protein such that the presence of DHDR protein or nucleic acid is detected in the biological sample. A preferred agent for detecting DHDR mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to DHDR mRNA or genomic DNA. The nucleic acid probe can be, for example, the DHDR nucleic acid set forth in SEQ ID NO:1, 3, 4, 6, 7, 9, 10, 12, 14, or 16, or the DNA insert of the plasmid deposited with ATCC as Accession Number _____, PTA-1845, _____, _____, ~~or~~ _____, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to DHDR mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

At page 89, lines 2 through 23, please replace the paragraph with the following amended paragraph::

The invention is based, at least in part, on the discovery of several human and mouse genes encoding novel proteins, referred to herein as DHDR-1, DHDR-2, DHDR-3 and DHDR-4. The entire sequences of human clones Fbh32142, Fbh21481, Fbh25964, and Fbh21686, and mouse clone m21481 were determined and found to contain open reading frames termed human "DHDR-1", "DHDR-2", "DHDR-3", and "DHDR-4", and mouse "DHDR-2", respectively, set forth in Figures 1, 6, 11, 16, and 31A, respectively. The amino acid sequences of these human and mouse DHDR expression products are set forth in Figures 1, 6, 11, 16, and 31B, respectively. The human DHDR-1 protein sequence set forth in SEQ ID NO:2 comprises about 802 amino acid residues and is shown in Figures 1A-1D. The human DHDR-2 protein sequence set forth in SEQ ID NO:5 comprises about 311 amino acid residues and is shown in Figures 6A-6B. The human DHDR-3 protein sequence set forth in SEQ ID NO:8 comprises about 369 amino acid residues and is shown in Figures 11A-11B. The human DHDR-4 protein sequence set forth in SEQ ID NO:11 comprises about 322 amino acid residues and is shown in Figure 16. The mouse DHDR-2 protein set forth in SEQ ID NO:15 comprises about 311 amino acid residues and is shown in Figure 31B. The coding regions (open reading frames) of SEQ ID NOs:1, 4, 7, 10, and 14 are set forth as SEQ ID NOs:3, 6, 9, 12, and 16. Clones ~~Fbh32142,~~ Fbh21481~~, Fbh25964, Fbh21686, and m21481~~, comprising the coding regions of human ~~DHDR-1,~~ DHDR-2, ~~DHDR-3, and DHDR-4, and mouse DHDR-2, respectively, were~~ was deposited

with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on _____, ~~May 9, 2000, _____, March 22, 2001, and _____, respectively,~~ and assigned Accession ~~Nos.~~ Number _____, ~~PTA-1845, _____, _____, or _____, respectively~~.